The influence of catastrophizing on treatment outcome in patients with non-specific low back pain: A systematic review

Wertli, Maria M ; Burgstaller, Jakob M ; Weiser, Sherri ; Steurer, Johann ; Kofmehl, Reto ; Held, Ulrike

Abstract: Study Design. Systematic reviewObjective. The aim of the current study was to assess the effect of catastrophizing on treatment efficacy and outcome in patients treated for low back pain.Summary of Background Data. Psychological factors including catastrophizing thoughts are believed to increase the risk for chronic low back pain. The influence of catastrophizing is debated.Methods. In September 2012 the following databases were searched: BIOSIS, CINAHL, Cochrane Library, Embase, OTSeeker, PeDRO, PsycInfo, Medline, Scopus, and Web of Science. For 50 of 706 references full text was assessed. Results based on 11 studies were included in this analysis.Results. In 11 studies, a total of 2,269 patients were included. Seven studies were of good and four of moderate methodological quality. Heterogeneity in study settings, treatments, outcomes, and patient populations impeded meta-analysis. Catastrophizing at baseline was predictive for disability at follow-up in four studies and for pain in two studies. Three studies found no predictive effect of catastrophizing. A mediating effect was found in all studies (n = 5) assessing the impact of a decrease in catastrophizing during treatment. A greater decrease was associated with better outcome. Most studies that investigated the moderating effects on treatment efficacy found no effect (n = 5). However, most studies did not look for a direct interaction between the treatment and catastrophizing thoughts. No study investigated the influence of catastrophizing on work-related outcomes including return to work.Conclusion. Catastrophizing predicted degree of pain and disability and mediated treatment efficacy in most studies. The presence of catastrophizing should be considered in patients with persisting back pain. Limited evidence was found for the moderating effects on treatment efficacy. Future research should aim to clarify the role of catastrophizing as a moderator of outcome and investigate its importance for work-related outcomes.

DOI: https://doi.org/10.1097/BRS.0000000000000110

Spine Publish Ahead of Print
DOI: 10.1097/BRS.0000000000000110

The Influence of Catastrophizing on Treatment Outcome in Patients with Non-Specific Low Back Pain – A Systematic Review

Maria M. Wertli M.D.[1,2], Jakob M. Burgstaller M.D., D.M.D.[1], Sherri Weiser Ph.D.[2], Johann Steurer M.D.[1], Reto Kofmehl BSc.[1], Ulrike Held Ph.D.[1]

[1] Horten Centre for Patient Oriented Research and Knowledge Transfer, Department of Internal Medicine, University of Zurich, Pestalozzistrasse 24, 8032 Zurich, Switzerland

[2] NYU Hospital for Joint Diseases, Occupational and Industrial Orthopaedic Center (OIOC), New York University, 63 Downing Street, New York, NY 10014, USA

Corresponding author:

Jakob M. Burgstaller, M.D., D.M.D.

Horten Centre for Patient Oriented Research and Knowledge Transfer, Department of Internal Medicine, University of Zurich, Pestalozzistrasse 24, 8091 Zurich, Switzerland

Phone: +41 44 255 87 09

Facsimile: +41 44 255 97 20

E-mail: jakob.burgstaller@usz.ch

Acknowledgment

This study was performed in collaboration with many experienced researchers and clinicians. We thank the research team of the Occupational and Industrial Orthopaedic Center (OIOC), New York University (NYU) Langone Medical Center in New York for their very valuable

discussions and input. Thanks are extended to Dr. Martina Gosteli, University of Zurich, for conducting the literature search.

The Manuscript submitted does not contain information about medical device(s)/drug(s).

No funds were received in support of this work.

No relevant financial activities outside the submitted work.

Abstract

Study Design: Systematic review

Objective: The aim of the current study was to assess the effect of catastrophizing on treatment efficacy and outcome in patients treated for low back pain.

Summary of Background Data: Psychological factors including catastrophizing thoughts are believed to increase the risk for chronic low back pain. The influence of catastrophizing is debated.

Methods: In September 2012 the following databases were searched: BIOSIS, CINAHL, Cochrane Library, Embase, OTSeeker, PeDRO, PsycInfo, Medline, Scopus, and Web of Science. For 50 of 706 references full text was assessed. Results based on 11 studies were included in this analysis.

Results: In 11 studies, a total of 2,269 patients were included. Seven studies were of good and four of moderate methodological quality. Heterogeneity in study settings, treatments, outcomes, and patient populations impeded meta-analysis. Catastrophizing at baseline was predictive for disability at follow-up in four studies and for pain in two studies. Three studies found no predictive effect of catastrophizing. A mediating effect was found in all studies (n=5) assessing the impact of a decrease in catastrophizing during treatment. A greater decrease was associated with better outcome. Most studies that investigated the moderating

effects on treatment efficacy found no effect (n= 5). However, most studies did not look for a direct interaction between the treatment and catastrophizing thoughts. No study investigated the influence of catastrophizing on work-related outcomes including return to work. *Conclusion:* Catastrophizing predicted degree of pain and disability and mediated treatment efficacy in most studies. The presence of catastrophizing should be considered in patients with persisting back pain. Limited evidence was found for the moderating effects on treatment efficacy. Future research should aim to clarify the role of catastrophizing as a moderator of outcome and investigate its importance for work-related outcomes.

Key words: low back pain; back pain; catastrophizing; fear avoidance; fear avoidance beliefs; fear avoidance model; prognosis; outcome; treatment outcome; mediator; moderator; predictor

Level of Evidence: 1

Mini Abstract

The literature about the effect of catastrophizing on treatment efficacy and outcome in patients treated for low back pain was systematically assessed. In 11 studies catastrophizing predicted degree of pain and disability and mediated treatment efficacy. Limited evidence was found for the moderating effects on treatment efficacy.

Key Points

This is a systematic review summarizing the effect of catastrophizing on treatment efficacy and outcome in patients treated for low back pain.

In 11 studies catastrophizing predicted degree of pain and disability and mediated treatment efficacy.

Limited evidence was found for the moderating effects on treatment efficacy.

The presence of catastrophizing should be considered in patients with persisting back pain.

Introduction

Patients' attitudes and coping mechanisms have been shown to play a causal role in the chronification of low back pain (LBP). Almost all adults once in their lifetime complain about LBP, but only 10-15 percent develop chronic LBP.[1] This small percentage of patients accounts for three-quarters of the costs of medical care and lost productivity associated with LBP.[2,3] There is consensus among experts to avoid unnecessary investigation and overtreatment of patients with acute LBP by treating symptomatically with encouragement to return to normal activity.[4] Persisting pain for several weeks strongly predicts the development of chronic low back pain, a condition where complete recovery and return to full physical function are often difficult to achieve.[5] Current research aims to identify risk indicators for delayed recovery in patients with sub-acute LBP in order to optimize treatment and avoid chronification. Targeted and timely interventions in patients at risk for chronic pain facilitate recovery and may reduce health care costs.[6]

The Fear Avoidance Model (FAM) is a theoretical model that describes how psychological factors affect the experience of pain and the development of chronic pain and disability.[7] Within this theoretical model, the presence of catastrophizing thoughts or behavior is a

prerequisite for poor outcome and is defined as "an exaggerated negative mental set brought to bear during actual or anticipated painful experience."[8] It is theorized that negative beliefs about pain and/or negative illness information leads to a catastrophizing response in which patients imagine the worst possible outcome. This leads to fear of activity and avoidance that in turn causes disuse and resultant distress, reinforcing the original negative appraisal in a deleterious cycle.[7] In chronic cases, catastrophizing may become a cognitive coping strategy based on the patient's characteristic coping style or because catastrophizing is believed to have prevented severe pain or other aversive outcomes in the past.[9] The FAM suggests that patients without catastrophizing and fear avoidance beliefs (FAB) are more likely to confront pain problems and are more active in the coping process. This type of "good" coping has been used to develop interventions for those high in catastrophizing and FAB.

Although there is some empirical support for the FAM, it is a matter of debate as to how and when to best assess catastrophizing in clinical practice. Current treatment guidelines for LBP recommend the timely identification and initiation of multidisciplinary treatment for other psychological factors (e.g. depression, distress, job dissatisfaction) associated with increased risk for delayed recovery.[10-12] Whether catastrophizing influences treatment outcome in patients with low back pain remains unclear.

To date, the role of catastrophizing on treatment efficacy in LBP has not been reviewed systematically. The aim of this review is to assess the influence of catastrophizing on treatment response in randomized controlled trials (RCTs) in patients with LBP.

Materials and methods

This systematic review follows the recommendation of the PRISMA statement (Figure 1) on conducting systematic reviews of RCTs.[13]

Literature Search

We identified all RCTs meeting our eligibility criteria published between January 1980 and September 2012. The following databases were search by an experienced librarian (XX): BIOSIS, CINAHL, Cochrane Library, Embase, OTSeeker, PeDRO, PsycInfo, Medline, Scopus, and Web of Science. Search terms for catastrophizing were identified in the literature (e.g. catastrophising, catastrophization, catastrophisation). Two detailed search strategies are depicted in Appendix 1. To ensure the completeness of the literature search, one reviewer (XX) conducted an electronic hand search of the six most often retrieved journals and added all potentially eligible references not retrieved by the systematic search. In addition, bibliographies of included studies relevant to the research question were searched and potential eligible references included in the full text review (inclusion and exclusion criteria applied).

Eligibility Criteria

All RCTs were considered eligible that met the following criteria: they reported results concerning patients seeking care for LBP, they assessed the influence of catastrophizing on treatment outcome, and they were published between January 1980 and September 2012. We focused on RCTs with at least 30 patients per group because of a concern about sample size. Assuming a reduction in perceived disability that was one-third greater in the treatment group when compared to the reference group, a sample size of 37 patients per group would be sufficient to detect the difference in allowing a drop-out rate of 15% (alpha 0.80, significance

level 0.05). No limits for the study setting or language of the publication were applied. Excluded were reports from conference proceedings.

Study Selection, Data Extraction and Synthesis

The bibliographic details of all retrieved articles were stored. Two reviewers (XX and XX) independently screened all references by title and abstract and reviewed full texts in all studies that met the pre-defined eligibility criteria. Disagreements were discussed and resolved by consensus or by third-party arbitration (XX). Alternative researchers with specific language proficiencies were approached for non-English language references.

Outcome Definition

All investigated outcomes were extracted and categorized into work-related (e.g. sick days, employment) and non-work-related outcomes (e.g. pain, perceived disability). Each method of outcome measurement was appraised with regards to their validity and reliability and was operationalized [e.g. perceived disability measured by Oswestry Disability Index (ODI)].

Quality Assessment

The internal validity of each study was assessed using the Scottish Intercollegiate Guidelines Network (SIGN) Methodology checklist for RCTs by the two reviewers independently (XX and XX).[14] Quality was rated as follows: *High (++):* most of the criteria have been fulfilled. If not fulfilled, the conclusions of the study are very unlikely to alter. *Moderate (+):* some criteria fulfilled. Criteria not adequately described are unlikely to alter the conclusions. *Low (-):* few or no criteria fulfilled. The conclusions are likely to alter.

As recommended by SIGN, studies rated by both reviewers as low quality were excluded from further analysis.

Operationalization of Catastrophizing as Predictor, Mediator, and Moderator

The definitions for predictor, mediator, and moderator were adopted from Pincus and colleagues:[15]

- Predictor: baseline catastrophizing affects outcome but does not interact with the allocated treatment intervention.
- Mediator: change in catastrophizing during treatment impacts outcome, with or without interacting with allocated treatment.
- Moderator: catastrophizing at baseline interacts with treatment.

The quality of the moderator analysis was assessed for each study by two reviewers (XX and XX) and discussed with an experienced statistician (XX). The following factors were considered: 1) Was the analysis a priori defined; 2) Was the selection of factors for the analysis clinically plausible; 3) Were moderators measured prior to randomisation; and 4) Was there an adequate quality of measurement of baseline factors, that contains an explicit test of the interaction between moderator and treatment?

Psychometric Properties and Description of the Questionnaires

The Pain Catastrophizing Scale (PCS) consists of 13 questions.[16,17] The score is a sum of all 13 items (each item on a scale of 0 – 4, range 0 – 52). The higher the score, the more catastrophizing thoughts are present. The internal consistency is high (Cronbach's alpha 0.87 to 0.95).[17-19] The three catastrophizing subscales are: rumination (sum of item 8, 9, 10, 11;

range 0 – 16), magnification (sum of items 6, 7, 13; range 0 – 12), and helplessness (sum of items 1, 2, 3, 4, 5, 12; range 0 – 24). The internal consistency is moderate to high (Cronbach's alpha: rumination 0.87 – 0.95, magnification 0.66 – 0.88, helplessness 0.78 – 0.91).[17,19]

The Coping Strategies Questionnaire (CSQ) consists of a 48-item checklist assessing six cognitive and two behavioral coping strategies.[9] Six questions assess catastrophizing (item 5, 12, 14, 28, 38, 42). The score is computed by summing responses to the six items (each item is scored 0 – 6 points, range 0 to 36). Internal consistency and reliability in a low back pain population was good in all sub-scales (Cronbach's alpha between 0.71 and 0.85.[9] The Cronbach's alpha of the catastrophizing subscale was between 0.78[9] and 0.84.[20]

The Pain-Related Self-Statements Scale (PRSS) is intended to assess situation-specific cognitions that either promote or hinder attempts to cope with pain.[21] Catastrophizing is assessed with the items 2, 4, 7, 9, 10, 13, 15, 16 and has been shown to be reliable and valid (Cronbach's alpha 0.83).[21] Items are scored on a Likert scale (0 to 5 points); the score is the average of all items (range 0 to 5). Higher values indicate more catastrophizing.

The Pain Cognition List (PCL) is a 50 item scale that measures a verbal-cognitive response system of chronic pain.[22] Catastrophizing is measured by 17 items (each item scored on a five-point Likert scale; 1: highly disagree to 5: totally agree). A sum score is obtained per subscale for each patient. The catastrophizing subscale (range 17 – 85) has been shown to be reliable and valid (Cronbach's alpha 0.88).[22,23]

The Pain Coping and Cognition List (PCCL) is a 42-item self-report questionnaire, developed on the basis of the PCL, CSQ, and MPLC (Multidimensional Pain Locus of Control Questionnaire) covering attributions, expectancies, and cognitive coping strategies. Each item is scored on a six-point Likert scale (1: totally disagree to 6: totally agree).

Catastrophizing is covered by one of the four subscales (12 items). The internal consistencies of the Catastrophizing subscale proved to be good (Cronbach's alpha 0.85).[24,25]

The PCS and the CSQ are considered to be equally reliable and valid for the measurement of catastrophizing thoughts.[26,27] It has therefore been proposed to use the PCS in research that aims to explore catastrophizing.[26] The PRSS is considered to be more pain-specific when compared to the CSQ. A direct comparison of the PRSS and the CSQ showed a moderately strong linear relationship between the two scales (r=0.56).[21] The correlation between the catastrophizing subscale of the PCL and the CSQ or PCS was high (r=0.70).[23]

Statistical analysis

Due to heterogeneous study populations, measurements, and scales used as well as outcomes investigated, only descriptive statistics were used to summarize findings across all cohort studies. Forest plots were generated based on values reported using R statistical software for Windows.[28]

Results

Study Selection

The search and inclusion process is summarized in Figure 1. Out of 1,473 records, 50 were reviewed in full text. The full text assessment utilizing the inclusion and exclusion criteria resulted in the exclusion of 37 studies.The main reasons for exclusion were are summarised in Figure 1. In total, 13 publications based on 11 RCTs were included in the analysis.

Study Characteristics

RCTs conducted in a general practitioner setting (GP, n=3), in rehabilitation clinics (n=3), hospitals / specialists (n=3), and physical therapy outpatient clinics (n=2) (baseline characteristics in Table 1). The study quality was good in seven and moderate in six studies (Appendix 2). The primary outcome in most RCTs was self-report measurements (i.e. pain, disability, change in pain or disability). No RCT investigated return to work or other work-related outcomes. Five publications (four RCTs) used the CSQ for assessing catastrophizing, [29-33] three the PCS (two RCTs),[34-36] two the PCL,[37,38] two the PRSS catastrophizing subscale,[39,40] and one the PCCL.[25] Cut-off values were only applied once (median split >11, ≤11).[31]

The Influence of Catastrophizing on Treatment Efficacy and Outcome

A summary of the predictor-, mediator-, and moderator-analyses is provided in Table 2. Catastrophizing at baseline predicted treatment outcome without interacting with the treatment in four RCTs,[29,34,36,38] but was not predictive in two other RCTs.[33,37] High catastrophizing was associated with more disability at follow-up in four RCTs [29,34,36,38] and with more pain in two RCTs.[36,38] Only one RCT failed to find an association between high catastrophizing scores and disability.[33] In this RCT, baseline catastrophizing was very low (mean CSQ 8.4 on a 0 to 36 point scale). Catastrophizing was not predictive for treatment satisfaction.[37]

In all five RCTs that investigated the mediating effects of a change in catastrophizing from baseline to follow-up, a decrease in catastrophizing was found to be associated more daily activity,[29] more internal pain control,[25] a greater decrease in highest level of pain (not for average pain or disability) in one RCT,[32] and more decrease in pain[35] and disability in another[34] (Table 3).

Catastrophizing moderated treatment efficacy in two publications based on one RCT[30,31] but not in five other RCTs.[29,34,37,39,40] One RCT found high catastrophizing scores to reduce treatment efficacy for usual care (UC) but not in the minimal intervention study (MIS) targeted to reduce pain-related fear and activity avoidance.[30,31] No moderating effect was found in three RCTs that compared exercise to cognitive behavioral approaches (CBT).[29,34,39] A detailed description of the study results is given in Appendix 3.

Discussion

Main Findings

In this systematic review of 11 randomized controlled trials (RCTs) on the effect of catastrophizing in patients with low back pain, we found catastrophizing to predict outcome for pain and disability in four RCTs. The RCTs that investigated mediating effects showed an association between a decrease in catastrophizing and an increase in daily activities and a decrease in pain. There was limited and conflicting evidence for the moderating effect of catastrophizing on treatment efficacy. No RCT assessed work-related outcomes.

The analysis of a moderator effect was inadequate in most RCTs and a final conclusion would be premature. All RCTs showing no moderating effect of catastrophizing included too few patients to detect a difference between the treatment arms. Therefore, any moderating effects could have been easily missed. Further, low catastrophizing at baseline could explain non-predictive findings. However, baseline values were not consistently associated with outcomes. Most RCTs did not look for a direct interaction test between the treatment and catastrophizing.

Results in Light of Existing Literature

The effect of catastrophizing on the outcome of treatment has received increasing attention.[41,42] To our knowledge this is the first systematic review that assessed the predictive, mediating, and moderating effect of catastrophizing in patients with low back pain. In surgical patients, catastrophizing has been associated with more post-surgical pain and poorer quality of life.[43] The influence of catastrophizing on outcome in patients undergoing non-surgical treatments has not been reviewed systematically. In a recent analysis of subgroups that might benefit from self-management programs in musculoskeletal pain, catastrophizing was identified as a moderator in one study.[44] The current analysis further expands the knowledge about the influence of catastrophizing in patients with low back pain on treatment efficacy and outcome. While there was a consistent association between higher catastrophizing and more disability and pain at follow-up, there is insufficient data available to analyze the influence of catastrophizing on work-related outcomes including return to work and sick days. Pain catastrophizing conceptually belongs to the fear avoidance model. It is believed that catastrophizing is a precursor of pain-related fear.[45] Fear avoidance beliefs decrease the treatment efficacy of treatments based on biomedical concepts (e.g. physical therapy) and increase treatment efficacy in treatments that aim to reduce fear avoidance beliefs (XX submitted). However, it is possible to have fear avoidance beliefs without catastrophizing.[46] To date it is not known if one can also have high catastrophizing and low fear avoidance beliefs.

Limitations

The main limitation is small sample sizes in most RCTs. None of the RCTs provided a power analysis for moderator effect and most RCTs did not conduct a direct test for any interaction between catastrophizing and treatment. The heterogeneity of studies and the methodological

limitations impeded the authors from conducting a meta-analysis. We have tried to balance these limitations by providing a comprehensive comparative description of all the RCTs included.

Implications for Research

Future research should aim at identifying the importance of catastrophizing in relation to fear avoidance beliefs and other psychological factors. Further, the influence of catastrophizing on treatment response in currently used treatment strategies in low back pain should be investigated. The current analysis suggests that any catastrophizing can be associated with worse outcome. It is unknown whether or not cut-off values can be applied to detect patients at high risk.

Implications for Practice

The findings of this review suggest that high catastrophizing scores are associated with more pain and disability at follow-up. It has been shown that catastrophizing may be modified with treatment and that a decrease during treatment is associated with better outcome.[25,38,47] Therefore measures that assess catastrophizing might be helpful in clinical practice to identify patients at risk for delayed recovery. Questionnaires used in the analysed RCTs consisted of at least six items. In a busy back pain patient clinic shorter screening tools are warranted. Stratified primary care management by using screening tools that incorporate catastrophizing among other psychological domain, e.g. the STarT Back Tool or the Orebro Questionnaire[48] has been shown to be effective and reduce costs.[6,49]

Conclusion

Catastrophizing thoughts were associated with more pain and disability at follow-up in patients with low back pain. A decrease in catastrophizing during treatment is associated with better outcome. Insufficient evidence was available for the assessment of moderating effects and no RCT investigated work-related outcomes.

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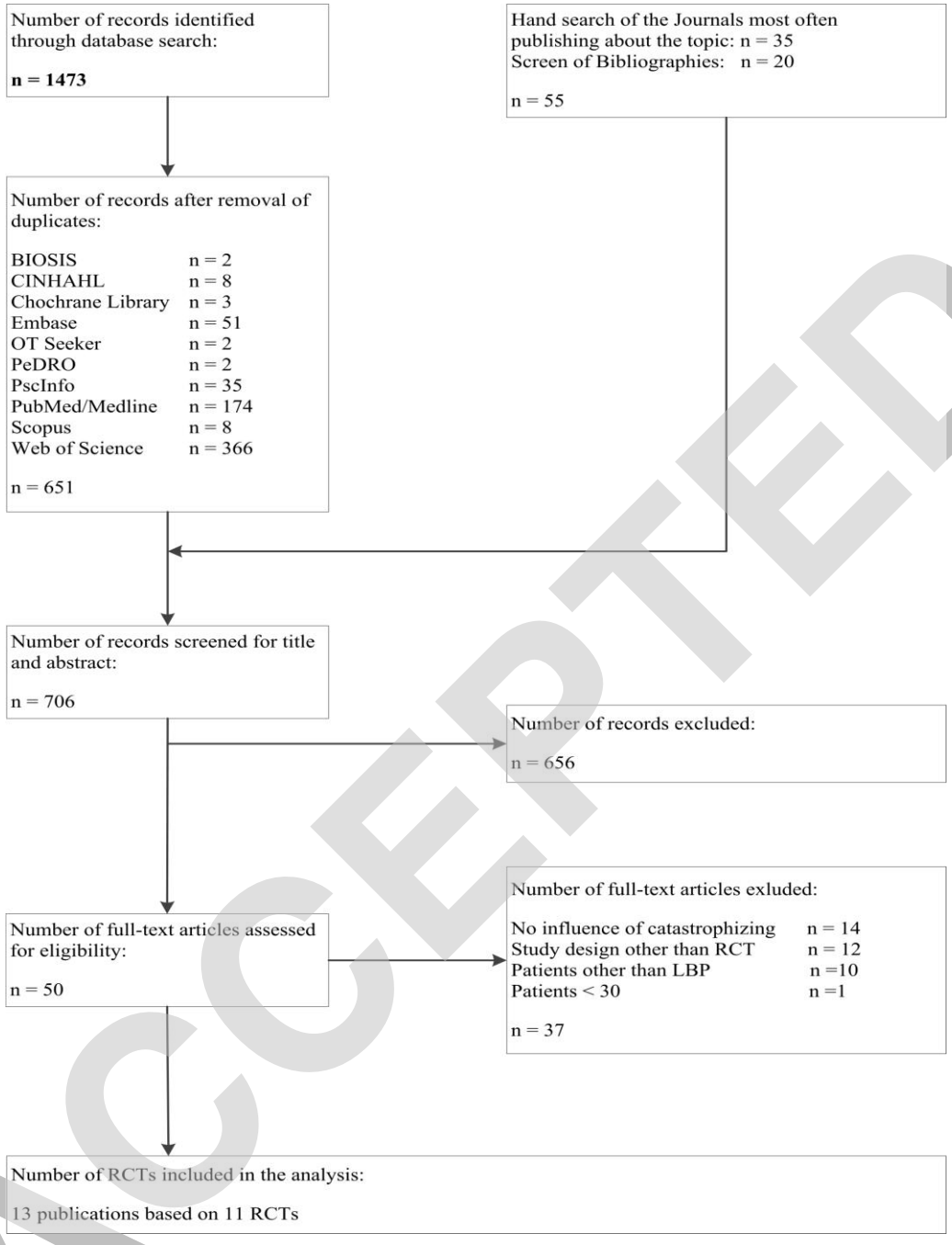

Figure 1: Exclusion criteria.

Table 1: Baseline characteristics of studies investigating Low Back Pain

Less than six months							
Study	**Setting**	**Diagnostic criteria**	**DD: days mean (SD)**	**Age mean (SD)**	**Treatment**	**n (f)**	**FU**
Jellema, Vlaeyen, 2006 [18]	Randomization on level GP practice. Participating GPs selected 10 consecutive patients, Netherlands	NSLBP, 14.6 % radiating below the knee	UC median 14 IQR (7-21) MIC 11 (5-21)	UC 42.0 (12); MIC 43.4 (11.1)	UC (n= 171) vs. MIC (n= 143)	314 (149)	6 weeks
Jellema, 2005 [19]	Same study as Jellema, Vlaeyen, 2006						52 weeks
Hancock, Davies, 2009 [10]	Patient presenting in 40 general practitioners working in primary practice across Sydney, Australia	NSLBP: 12. rib to buttock crease with moderate pain and moderate disability (SF-36, item 7/8)	9.13 (9.31)	40.7 (15.6)	Spinal manipulation + Diclofenac / Placebo (n= 119) vs. Placebo Spinal manipulation + Diclofenac / Placebo (n= 120)	239 (105)	Time to recovery
Smeets, 2009 [40]	Recruitment by clinician referral, advertisement, waiting list PT clinics, treatment in 7 physiotherapy clinics in Australia and New Zealand	NSLBP ≥6 weeks but ≤12 weeks	42-56 (48%), 63-77 (37%), >84 (15%)	49.9 (15.8)	EA (n= 63) vs SEA (n= 63) vs ESA (n= 65) vs SESA (n= 68)	259 (124)	1 year
George, Zeppieri, 2008 [9]	Patients referred for rehabilitation to three participating University of Florida affiliated clinics, U.S.A.	NSLBP + SLBP Quebec Task Force on Spinal Disorders (QTFSD). Leg pain TBC 38%, GA 49%, GX 42%	TBC 47 (34), TBC + GA 41 (39), TBC + GX 69 (49)	37.5 (14.9)	Treatment-based classification (TBC) physical therapy vs. TBC + graded activity (GA) vs. TBC + graded exposure (GX)	108 (74)	1 and 6 months
Beneciuk, 2012 [3]	Same study as George, Zeppieri 2008						
Hill, 2008 [13]	Patient recruited from 28 general practices, treated by trial physio-therapists, North Staffordshire, UK	NSLBP ≤12 weeks for the first or second time	≤12 weeks	40.65 (11.8)	Pain management program or PT + manipulation	402 (210)	1 year

Wessels, 2007 [53]	Patients recruited from several hospitals, treatment setting n.r., Germany	NSLBP. At least 1 LBP episode in the last 2 years	n.r.	40 (11.1)	Multidisciplinary program (n= 80) vs. exercise program (n= 82)	162 (150)	Posttreatment (13 weeks)
More than 6 months							
Study	**Setting**	**Diagnostic criteria**	**DD**	**Age mean (SD)**	**Treatment**	**n (f)**	**FU**
Leeuw, 2008 [24]	Patients recruited via 9 various outpatient facilities or newspaper-ad, treated in 4 outpatient rehabilitation centers, Netherlands	NSLBP ≥3 months, RDQ >3, TSK >33	9.0 years (9.4)	45.3 (9.45)	Exposure in vivo (n= 42) vs GA (n= 43)	85 (41)	6 months
Oosterhof, 2008 [30]	Patients referred by family doctor or medical specialist to the Pain Centre of Radboud University Medical Centre Nijmegen, Netherlands	NSLBP ≥6 months	6.4 years (0.6)	50.2 (1.1)	TENS (n= 81) vs sham TENS (n= 82)	165 (97)	10 days
Smeets, 2006 [41]	Patients referred by GPs and medical specialists to 3 Dutch outpatient rehabilitation centers	NSLBP ≥3 months, ability to walk at least 100m without interruption	4.8 years (6.1)	41.81 (9.92)	APT (n= 52) vs CBT (n= 55) vs CT (n= 55) vs WL (n= 49)	227 (105)	70 days
Mannion, 1999 [27]	Hospital based outpatient treatment (PT), recruitment by advertisement, Switzerland	NSLBP ± referred pain (non-radicular), continual or recurrent, ≥3 months, causing absence from work or solicitation of medical attention	10.9 years (9.4)	45.1 (10.0)	Modern active PT (n= 49) vs. muscle conditioning on training devices (n= 49) vs. low-impact aerobics (n= 50)	148 (84)	6 months
Spinhoven, 2004 [42]	Patients referred by GPs and medical specialists to Hoensbroeck Rehabilitation Center, Netherlands	NSLBP ≥6 months	10.1 months (8.7)	40.0 (9.2)	OPCO (n= 59) vs OPDI (n= 58) vs WLC (n= 31)	159 (94)	1 year

LBP: low back pain; NSLBP, non-specific low back pain; SLBP, specific low back pain; PF, prognostic factor reporting of the total of 16 possible domains; SIGN, SIGN quality rating: ++ high quality, + moderate quality;

DD, Disease Duration; FU, Follow-up; TBC, treatment-based classification; GA: graded activity; GX, graded exposure; PT, physical therapy; UC, usual care; MIS, minimal intervention strategy; AM, active management; CBT, cognitive behavioral therapy; APT, active physical therapy; CT, combined therapy; WL, waiting list; GivE, Graded in vivo exposure; QA, Questionnaire used; FAB, Fear Avoidance Beliefs; FABQ, fear avoidance questionnaire; FABQ-P, FABQ physical activity sub-scale; FABQ-W: FABQ work sub-scale; TSK: Tampa Scale of Kinesiophobia; OR, odds ratio; MA, multiple regression analysis; IQR: interquartile range; CMID, clinical meaningful important difference; Log. Reg., logistic regression; U.L., univariante logistic regression; L.R., linear regression; ODI, Oswestry Disability Index: higher score indicates more disability: CMID = ≥12 points reduction; RTW, return to work; CPG, chronic pain grade (von Korff) questionnaire: higher score indicates more pain; GCP, graded chronic pain scale; PDI, pain disability index (Pollard, 1984): higher score indicates more disability; RMQ, Roland Morris Questionnaire: higher score indicates more disability: CMID = ≥2-3 point reduction, ≥30% change; SF-36D, physical health sub-score: higher score indicates higher level of functioning; SF-36M, mental health sub-score: higher score indicates higher level of functioning; EA, exercise + advice; SEA, sham exercise + advice; ESA, exercise + sham advice; SESA, sham exercise + sham advice; OPCO, operant behavioral treatment and cognitive coping skills training; OPDI, operant behavioral treatment and group discussion; WLC, waiting-list control condition

Table 2: Summary of the effect of catastrophizing as predictor, mediator and moderator

Less than six months					
Study Year	**Scale: mean (SD)**	**Predictor**	**Mediator**	**Moderator**	
Jellema, Vlaeyen, 2006 [18]	CSQ 11.8 (6.7)	Ø	Ø	+ Moderator in UC (OR 0.94, 95% CI, 0.89 – 0.99)	– No moderator in MIS (OR n.r.)
Jellema, 2005 [19]	CSQ 11.8 (6.7)	Ø	Ø	+ High catastrophizing (>11) in MIS more recovery than in UC (OR 0.72, 95% CI, 0.29 – 1.80) Low catastrophizing (≤11) in MIS less recovery than in UC (OR 1.84, 95% CI, 0.80 – 4.22)	
Hancock, Davies, 2009 [10]	PRSS 1.85 (scale 0-5)	Ø	Ø	– No interaction of catastrophizing with treatment (NSAID vs. placebo) on pain and recovery	
Smeets, 2009 [40]	PRSS 18 (9)	Ø	Ø	– No significant influence of catastrophizing on exercise or advice for pain and disability	
George, Zeppieri, 2008 [9]	PCS range 12.6 - 20.7	Ø	+ Decrease in catastrophizing associated with more pain decrease (β 0.38, 95% CI, 0.09 – 0.67)	Ø	

Beneciuk, 2012 [3]	PCS 16.3 (11.2)	+ High catastrophizing with high fear avoidance beliefs associated with more pain and disability in all treatment groups ($p<0.05$)	Ø	Ø
Hill, 2008 [13]	CSQ 8.4 (6.7)	– Catastrophizing not associated with disability after .12 months (univariante OR 1.77, 95% CI, 1.13 – 2.75; multivariante n.r.)	Ø	Ø
Wessels, 2007 [53]	Ø	+ Catastrophizing interferes with daily activity at 3 months (β 0.25, 95% CI, 0.12 – 0.35)	+ Decrease in catastrophizing explains 2.5% of total variability in outcome (MPI-D) (β 0.236, 95% CI, 0.12 – 0.35)	– No significant interaction between catastrophizing and treatment ($p = 0.06$)
More than 6 months				
Study Year	**Scale: mean (SD)**	**Predictor**	**Mediator**	**Moderator**
Leeuw, 2008 [24]	PCS 22.9 (10.4)	+ More catastrophizing is associated with more disability at 6 months (QPDBS β 0.43, 95% CI, 0.25 – 0.61; PSC β 0.70, 95% CI, 0.41 – 0.99)	+ Decrease in catastrophizing significantly mediated the effect of EXP relative to GA on disability and main complaint. Results n.r.	– No significant interaction between catastrophizing and treatment (criteria for inclusion $p <0.10$)
Oosterhof, 2008 [30]	PCL 43.9 (SE 1.2)	– Catastrophizing no influence on treatment satisfaction after 10 days	Ø	– Catastrophizing no influence on treatment satisfaction (values n.r.)
Smeets, 2006 [41]	PCL 39 (12)	+ Catastrophizing associated with more pain and disability in all treatment groups (APT, CBT and CT) after 2 months	Ø	Ø
Mannion, 1999 [27]	Ø	Ø	+ Decrease in catastrophizing explains 23% decrease in greatest pain but not decrease in average pain and disability	Ø
Spinhoven, 2004 [42]	PCCL 40.5 (9)	Ø	+ Decrease in catastrophizing increases internal pain control (β 0.20, $p < 0.05$)	Ø

Scale ranges: PCS 0 - 52, CSQ 0 - 36, PRSS 0 - 45, PCL 17 - 85, PCCL 12 – 72; Ø, not investigated; UC, usual care; MIS, minimal intervention strategy; CBT, cognitive behavioral therapy; APT, active physical therapy; CT, combined therapy; FAB, Fear Avoidance Beliefs; MPI-D, German version of the West Haven Multidimensional Pain Inventory

Table 3: Moderating effect of catastrophizing on treatments

Study Year	**Moderating effect on Treatment**	**Test of interaction**	**Disease Duration**	**n**	**FU (weeks)**	**Outcome**
Jellema, 2006 [18] + 2005 [19]	Catastrophizing reduces treatment effect in Group 1: UC: guideline GP based care; but not in Group 2 MIS: GP provided information and advice for self-care + Back Book	no	acute - subacute	314	52	Non-work related: RMQ
Hancock, Davies, 2009 [10]	No effect on NSAID vs. Placebo Group 1: Placebo + placebo manipulation Group 2: Diclofenac + placebo manipulation Group 3. Placebo + spinal manipulation Group 4: Diclofenac + manipulation	yes	acute	240	12	Non-work related: Number of days to recovery
Smeets, 2009 [40]	No effect on all treatment groups: Group 1: CBT informed progressive exercise and PT advice stay active and addressing helpful beliefs Group 2: CBT informed exercise + sham advice Group 3: Sham exercise + advice Group 4: Sham exercise + sham advice	no	subacute	259	52	Non-work related: Δ pain (NRS) + Δ disability (PSFS)
Wessels, 2007 [53]	No interaction between catastrophizing and treatment: Group 1: Exercise Group 2: multidisciplinary prevention program including CBT, work hardening, back school	no	subacute - chronic	162	13	Non-work related: MPI-D
Leeuw, 2008 [24]	No interaction between catastrophizing and treatment: Group 1: operant behavioral GA: functional treatment goals, 2 psychological sessions Group 2: EXP: CBT techniques by using PHODA to identify fear hierarchy	yes	chronic	85	26	Non-work related: QBPDS PSC
Oosterhof, 2008 [30]	No influence on Group 1 TENS, and Group 2: Sham TENS	yes	chronic	165	10	Non-work related: treatment satisfaction

TENS, transcutaneous electrical nerve stimulation; UC, usual care; MIS, minimal intervention strategy; CBT, cognitive behavioral therapy; APT, active physical therapy; CT, combined therapy; PT, physical treatment; PHODA, Photograph Series of Daily Activities; FAB, Fear Avoidance Beliefs; MPI-D, German version of the West Haven Multidimensional Pain Inventory; RMQ, Roland and Morris Disability Questionnaire; QBPDS, Quebec Back Pain Disability Scale; PSC, Patient Specific Complaints; NRS, Numeric Rating Scale; PSFS, Patient-Specific Functional Scale

Appendix 1: Search History for PubMed, CINAHL, PsychINFO October Week 2 2012

Ovid MEDLINE(R), Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid OLDMEDLINE(R) 1946 to Present

#	Query	Results
1	exp Low Back Pain/	12474
2	((low or lower) adj3 ("back pain" or "back pains" or "back ache" or "back aches" or backache*)).ti,ab.	16245
3	((lowback or lumbal or lumbar or lumbosacral) adj3 (pain* or ache* or syndrome)).ti,ab.	3488
4	(lumbago or lumbalgia or lumbalgesia or (lumbosacroiliac adj3 strain)).ti,ab.	1221
5	or/1-4	23882
6	exp Catastrophization/	183
7	(catastrophizing or catastrophising or catastrophization or catastrophisation).mp. [mp=title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]	1111
8	(catastrophic adj3 (thinking or thought*)).ti,ab.	131
9	(pain adj3 (catastrophizer* or catastrophiser*)).ti,ab.	20
10	or/6-9	1185

11	5 and 10	179
12	limit 11 to yr="1980 -Current"	179
13	limit 12 to animals	0

PsycINFO 1806 to October Week 2 2012 (Ovid)

#	**Searches**	**Results**
1	back pain/ and (low or lower).ti,ab.	1870
2	((low or lower) adj3 ("back pain" or "back pains" or "back ache" or "back aches" or backache*)).ti,ab.	2206
3	((lowback or lumbal or lumbar or lumbosacral) adj3 (pain* or ache* or syndrome)).ti,ab.	176
4	(lumbago or lumbalgia or lumbalgesia or (lumbosacroiliac adj3 strain)).ti,ab.	26
5	or/1-4	2534
6	(catastrophizing or catastrophising or catastrophization or catastrophisation).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	1144
7	(catastrophic adj3 (thinking or thought*)).ti,ab.	150
8	(pain adj3 (catastrophizer* or catastrophiser*)).ti,ab.	25
9	or/6-8	1222
10	5 and 9	129
11	limit 10 to yr="1980 -Current"	129

Appendix 2: Internal Validity of Studies (SIGN methodology checklist) [11] and assessment of moderators [33]

Study	**Year**	**SIGN**											**Moderators**				
		1.1	**1.2**	**1.3**	**1.4**	**1.5**	**1.6**	**1.7**	**1.9**	**1.10**	**2.1**	**3.1**	**A**	**B**	**C**	**D**	**E**
Wessels	2007	WC	WC	NR	NR	WC	WC	WC	NA	NA	+	-	NF	Yes	No	Yes	No
Jellema	2006	WC	WC	NA	PA	WC	WC	WC	PA	NA	+	G	NF	Yes	No*	Yes	No
Jellema	2005	WC	WC	NA	PA	WC	WC	WC	PA	NA	+	G	NF	Yes	No*	Yes	No
Leeuw	2008	WC	WC	WC	AA	WC	WC	WC	WC	NA	+	G+O	NF	Yes	Yes	Yes	Yes
Oosterhof	2008	WC	WC	WC	WC	WC	WC	AA	WC	NA	++	G	NF	Yes	No	Yes	Yes
Smeets	2009	WC	WC	WC	WC	WC	WC	AA	WC	NA	++	G	Yes	Yes	Yes	Yes	No
Smeets	2006	WC	WC	WC	WC	WC	WC	WC	WC	NA	++	O	NF	Yes	Yes	Yes	No
Mannion	1999	WC	WC	NA	AA	WC	WC	WC	WC	N/A	++	G+O	NF	Yes	No	Yes	Yes*
Spinhoven	2004	WC	WC	WC	WC	WC	WC	WC	WC	NA	++	H	NF	Yes	No	Yes	Yes*
Hill	2008	WC	WC	WC	WC	WC	WC	WC	WC	NA	++	N+O	NF	Yes	Yes	Yes	No
Hancock	2009	WC	WC	WC	WC	WC	WC	WC	WC	NA	++	H+G	NF	Yes	Yes	Yes	Yes*
George	2008	WC	WC	WC	WC	WC	WC	WC	WC	NA	+	-	NF	Yes	Yes	Yes	No
Beneciuk	2012	WC	WC	WC	WC	WC	WC	WC	WC	NA	+	-	NF	Yes	Yes	Yes	No

WC, well covered; AA, adequately addressed; PA, poorly addressed; NA, not addressed; NR, not reported; N/A, not applicable; Yes*, yes (not significant); No*, no (cluster)

quality: most of the criteria have been fulfilled. If not fulfilled, the conclusions of the study are very unlikely to alter; (+), moderate quality: some criteria fulfilled. Criteria not adequately described are unlikely to alter the conclusions; (-), low quality: few or no criteria fulfilled. The conclusions are likely to alter. 3.1 Funding: A, academic institution; H, healthcare industry; G, government; N, NGO; P, public funds; O, others; -, none

Moderators
A, a-priori analysis; B, selection of factors for analysis clinically plausible; C, moderators measured prior to randomisation; D, adequate quality of measurement of baseline factors; E, explicit test of the interaction between moderator and treatment

Appendix 3: Results of all included studies

Study	**Year**	**Therapy**	**Follow-up (days)**	**Outcome**	**Question-naire**	**Measure or cut-off used**	**MA?**	**Criteria for inclusion in MA**	**Measure reported**	**value**	**CI (5)**	**CI (95)**	**p**
Wessels	2007	all	91	inteference with daily life West Haven Multidimensional Pain Inventory German Version (MPI-D)	d_CSQ cat (0-36)	no	yes	first step: partial correlation coefficients, p<0.2 included sec step: regression analysis with changes in interference	Beta	0.205	0.10	0.31	<0.0001

Wessels	2007	all	91	inteference with daily life West Haven Multidimensional Pain Inventory German Version (MPI-D)	CSQ cat (0-36)	no	yes	first step: partial correlation coefficients, p<0.2 included sec step: regression analysis with changes in interference	Beta	0.236	0.12	0.35	<0.0001
Wessels	2007	cat x treatment	91	inteference with daily life West Haven Multidimensional Pain Inventory German Version (MPI-D)	CSQ cat (0-36) x treatment	no	yes	first step: partial correlation coefficients, p<0.2 included sec step: regression analysis with changes in interference	n.r.	n.r.	n.r.	n.r.	0.06
Jellema	2006	UC	364	≥ 30% improvement in Roland and Morris Disability Questio	CSQ cat (0-36)	no	yes	p<0.20	OR	0.94	0.89	0.99	0.03

				nnaire (RMQ)									
Jellema	2006	MIS	364	≥ 30% improvement in Roland and Morris Disability Questionnaire (RMQ)	CSQ cat (0-36)	no	no	p<0.20	n.r.	n.r.	n.r.	n.r.	n.r.
Jellema	2005	MIS vs UC	364	no recovery (7 point Likert-scale)	CSQ cat (0-36)	ms ≤11	yes		OR	1.84	0.80	4.22	
Jellema	2005	MIS vs UC	364	no recovery (7 point Likert-scale)	CSQ cat (0-36)	ms >11	yes		OR	0.72	0.29	1.80	
Leeuw	2008	all	180	QBPDS (Quebec Back Pain Disability Scale)	PCS (0-52)	no	yes	predefined	Beta	0.43	0.25	0.61	<0.001
Leeuw	2008	all	180	PSC (Patient Specific Complaints)	PCS (0-52)	no	yes	predefined	Beta	0.7	0.41	0.99	<0.001
Mannion	1999	all	180	ΔRMQ	CSQ cat (0-	no	yes	simple correlation	n.r.	n.r.	n.r.	n.r.	n.r.

					36)								
Mannion	1999	all	180	Δ in greatest pain (VAS)	CSQ cat (0-36)	no	yes	simple correlation	n.r.	n.r.	n.r.	n.r.	n.r.
Mannion	1999	all	180	Δ average pain (VAS)	CSQ cat (0-36)	no	yes	simple correlation	n.r.	n.r.	n.r.	n.r.	n.r.
Oosterhof	2008	all	10	proportion of patients satisfied with the initial treatment results and willing to continue (yes or no)	PCL cat (17-85)	no	yes, multiple regression model	r^2 increases at least 0.01 for pain (VAS)	n.r.	n.r.	n.r.	n.r.	
Smeets	2009	all	360	change in pain (11-point scale)	PRSS cat (0-45)	1 SD inc (9 points)	no	clinical relevant effect modification (1 SD change)	Mean	0.54	0.35	0.73	<0.001
Smeets	2009	ex	360	change in pain (11-point scale)	PRSS cat (0-45)	1 SD inc (9 points)	yes	clinical relevant effect modification (1 SD change)	Mean	-0.07	-0.62	0.48	

Smeets	2009	adv	360	change in pain (11-point scale)	PRSS cat (0-45)	1 SD inc (9 points)	yes	clinical relevant effect modification (1 SD change)	Mean	-0.24	-0.80	0.31	
Smeets	2009	all	360	change in patient-specific functional scale (0-10)	PRSS cat (0-45)	1 SD inc (9 points)	no	clinical relevant effect modification (1 SD change)	Mean	-0.31	-0.50	-0.12	0.001
Smeets	2009	ex	360	change in patient-specific functional scale (0-10)	PRSS cat (0-45)	1 SD inc (9 points)	yes	clinical relevant effect modification (1 SD change)	Mean	-0.26	-0.79	0.27	
Smeets	2009	adv	360	change in patient-specific functional scale (0-10)	PRSS cat (0-45)	1 SD inc (9 points)	yes	clinical relevant effect modification (1 SD change)	Mean	0.14	-0.40	0.68	
Smeets	2006	all	70	Roland and Morris Disability Questionnaire (RMDQ)	PCL cat		successful multilevel regression analysis 3-step method	differences baseline p<0.10, mediating = p<0.05	n.r.				

Smeets	2006	APT vs WL	70	Roland and Morris Disability Questionnaire (RMDQ) without catastrophizing	PCL cat (17-85)	no	yes		Beta	-2.415	-2.53	-2.30	
Smeets	2006	CBT vs WL	70	Roland and Morris Disability Questionnaire (RMDQ) without catastrophizing	PCL cat (17-85)	no	yes		Beta	-3.14	-3.26	-3.02	
Smeets	2006	CT vs WL	70	Roland and Morris Disability Questionnaire (RMDQ) without catastrophizing	PCL cat (17-85)	no	yes		Beta	-2.524	-2.64	-2.41	
Smeets	2006	APT vs WL	70	Roland and Morris Disability Questionnaire (RMDQ	PCL cat (17-85)	no	yes, multilevel regression	n.r.	Beta	-1.284	-1.39	-1.18	

				) with catastrophizing									
Smeets	2006	CBT vs WL	70	Roland and Morris Disability Questionnaire (RMDQ) with catastrophizing	PCL cat (17-85)	no	yes, multilevel regression	n.r.	Beta	-2.217	-2.32	-2.11	
Smeets	2006	CT vs WL	70	Roland and Morris Disability Questionnaire (RMDQ) with catastrophizing	PCL cat (17-85)	no	yes, multilevel regression	n.r.	Beta	-1.636	-1.74	-1.53	
Smeets	2006	APT vs WL	70	Current pain (VAS) without catastrophizing	PCL cat (17-85)	no	yes		Beta	-9.282	-9.84	-8.72	
Smeets	2006	CBT vs WL	70	Current pain (VAS) without catastrophizing	PCL cat (17-85)	no	yes		Beta	-15.826	-16.39	-15.27	
Smeets	2006	CT vs WL	70	Current pain (VAS) without	PCL cat (17-85)	no	yes		Beta	-8.685	-9.24	-8.13	

				catastrophizing								
Smeets	2006	APT vs WL	70	Current pain (VAS) with catastrophizing	PCL cat (17-85)	no	yes, multilevel regression	n.r.	Beta	-4.703	-5.23	-4.18	
Smeets	2006	CBT vs WL	70	Current pain (VAS) with catastrophizing	PCL cat (17-85)	no	yes, multilevel regression	n.r.	Beta	-12.165	-12.69	-11.64	
Smeets	2006	CT vs WL	70	Current pain (VAS) with catastrophizing	PCL cat (17-85)	no	yes, multilevel regression	n.r.	Beta	-5.124	-5.64	-4.61	
Spinhoven	2004	all	360	McGill Pain Questionnaire (MPQ), pain rating index	d_PCCL cat	no	Hirarchi-cal regression, residualized gain score	zero-order correlation	Beta	0.2	0.00	0.40	<0.05
Hill	2008	all	360	Higher than median value RMQ (≥3) at 12	CSQ cat	no	yes	p<0.05	OR	1.77	1.13	2.75	

				months									
Hancock	2009	NSAID vs Placebo	84	Number of days to recovery (1 day without pain = recovery)	PRSS cat (0-5)	no	yes	p<0.25	HR	1.095	0.80	1.49	0.567
George	2008	all	180	change at 6 months in NRS (Numerical Rating Scale)	d_PCS (0-52)	no	yes		Beta	0.38	0.09	0.67	<0.01
Beneciuk	2012	PT + CBT vs PT only	180	Disability (ODI)	PCS (0-52)	cat + FAB-P (<14) low	yes, Discriminant Function analysis, Cluster Analysis	N/A	Mean	-4.7	-17.24	7.84	
Beneciuk	2012	PT + CBT vs PT only	180	Disability (ODI)	PCS (0-52)	FAB-P (≥14) high	yes, Discriminant Function analysis,	N/A	Mean	3.6	-14.16	21.36	

							Cluster Analysis						
Beneciuk	2012	PT + CBT vs PT only	180	Disability (ODI)	PCS (0-52)	cat + FAB-P (≥14) high	yes, Discriminant Function analysis, Cluster Analysis	N/A	Mean	-16.9	-38.04	4.24	
Beneciuk	2012	PT + CBT vs PT only	180	Pain Intensity (NRS)	PCS (0-52)	cat + FAB-P (<14) low	yes, Discriminant Function analysis, Cluster Analysis	N/A	Mean	0.1	-2.17	2.37	
Beneciuk	2012	PT + CBT vs PT only	180	Pain Intensity (NRS)	PCS (0-52)	FAB-P (>= 14) high	yes, Discriminant Function analysis, Cluster Analysis	N/A	Mean	1	1.91	3.91	

Beneciuk	2012	PT + CBT vs PT only	180	Pain Intensity (NRS)	PCS (0-52)	cat + FAB-P (≥14) high	yes, Discriminant Function analysis, Cluster Analysis	N/A	Mean	-1.3	-4.09	1.49	

ms, median split